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May 22, 2107

Meeting Notes: Interagency Meeting (FDA, EPA, CDC, NIH, BARDA) with Oxitec/Intrexon
May 17, 2017

Overview

Oxitec left the meeting with a clear sense that:
1) The interagency group in person and on the phone recognized that a public health emergency continues to exist at this time but may not persist
2) OX513A represents an important potential tool for controlling *Aedes aegypti*
3) FDA and EPA have been working closely together and with Oxitec, and have previously identified options for the most expeditious regulatory path forward, for conducting a field trial. FDA and EPA reiterated those options, as well as their commitment to continue working toward expediting reviews, where appropriate, and ensuring a smooth transition to EPA at the appropriate time.
Much of the discussion was a reiteration of advice and options for regulatory pathways that FDA and EPA had previously communicated to the company individually and in joint FDA-EPA meetings with the company.

Oxitec indicated their interest in working with the USG to identify the most efficient regulatory pathway that would allow them to start mosquito release testing as soon as possible..
Regulatory jurisdiction of the Oxitec product is currently with FDA, but FDA and EPA have been working together to clarify that regulatory oversight of products intended to control mosquito populations resides with EPA. As such, draft FDA Guidance #236 is intended to clarify that GE mosquitoes intended for population control would be regulated as pesticides under EPA's Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). EPA and FDA representatives reiterated that the agencies are working closely together and will continue to do so to ensure smooth transition.
Oxitec has an Investigational New Animal Drug (INAD) file open with FDA that could allow for a field trial of mosquito releases relatively soon. However, Intrexon/Oxitec is concerned that timing of the transfer of jurisdiction could either delay releases or cause releases to be abruptly stopped.
EPA representatives reiterated that the company could at any time submit an application for an Experimental Use Permit (EUP) under FIFRA section 5. EPA could review the application and make a determination on whether to issue an EUP based on the information contained in the application. EPA could issue a determination on the EUP application even if FDA Guidance #236 has not been finalized.

From the open discussion during the meeting, Intrexon/Oxitec felt that it might be able start mosquito releases sooner under FDA's INAD regulatory mechanism than under the EPA mechanisms discussed because generation of protein characterization data requested by EPA in a previous meeting would be needed prior to issuance of an EUP and thus prior to initiating mosquito release testing. The group discussed continuing to move forward with plans for a field trial under FDA's jurisdiction, and simultaneously submitting an EUP application and data to EPA that would support the EUP and/or Section 18 assessments needed for releases under an EPA EUP or Section 18. The company and EPA agreed to expedite the scientific dialogue to get the needed data into EPA as soon as possible.
With regard to the FDA EUA regulatory mechanism, FDA emphasized its previous advice to Oxitec that, under the current circumstances, EUA would not necessarily be a faster mechanism to begin mosquito releases and that doing field releases under INAD or EPA's Section 18 or EUP still seem to be the more expeditious mechanisms.

Oxitec representatives indicated that completing all the protein characterization data EPA indicates it needs would take 6 months and data generation would likely be completed in October 2017. EPA committed to provide feedback to Oxitec as to whether all the protein data EPA had previously advised

should be submitted to support an EUP was essential for EPA to do risk assessments supporting an EUP or Section 18.

In response to an Oxitec comment on the timing of issuance of the EUP, EPA representatives noted that under PRIA (FIFRA fee for service provisions), the time allotted to complete an EUP review is 7 months. However, EPA noted again, as it did before, that EPA will work to issue an EUP sooner than 7 months after receiving the application and noted that how quickly it could complete the review depended in part on the contents of the application.

As previously explained to Oxitec, EPA representatives noted that the other pathway open to the company is a FIFRA Section 18 action. While the purpose of a Section 18 Emergency exemption is to respond to an emergency situation, Oxitec could collect/generate data as a component of that action. Although EPA can begin reviewing the Section 18 application, EPA would not be able to issue the Section 18 until FDA Guidance #236 is finalized and jurisdiction can transfer to EPA.
Furthermore, CDC encouraged Oxitec to work toward the EPA section 3 registration because if the emergency situation was declared over (like Brazil and WHO have already done, and Puerto Rico that is poised to do so), any emergency mechanisms might need to be terminated, as well. This could translate into the possibility that an emergency situation may not be in place for Florida and/or other locations moving forward.

EPA, FDA and Oxitec discussed paths forward, given the regulatory options:
Oxitec indicated that because of the time needed to complete the protein studies, they would prefer to continue to pursue the current process for investigational trials under FDA new animal drug authorities at this time, while also pursing available EPA pathways in preparation for transfer to EPA authority when FDA's Guidance #236 is final.

The group also reflected on the possibility of a multi-phased approach for the 2017-2018 field study where there would be a "natural break" in mosquito releases built into the study design. FDA and EPA had previously asked Oxitec whether the study design involved a natural stopping point or pause in mosquito releases, and the agencies had discussed such an approach with the company at previous meetings. Under such an approach, Oxitec suggested that a viable path would be where testing with field trials could occur under FDA INAD oversight during the Summer/Fall of 2017 with an EPA EUP submission sometime in the Fall of 2017 and EUP issuance (and transfer of jurisdiction) occurring in February 2018 for field trial oversight in the Spring/Summer 2018 under an EPA EUP.

Oxitec indicated that it had been in communication with FDA concerning the appropriate contents of an EA as part of an INAD submission to FDA, in particular the revisions needed to the package to more completely address potential endangered species (ESA) considerations. Oxitec indicated it anticipated submitting the full package to FDA by the end of May 2017. FDA stated it would do its best to review Oxitec's submission expeditiously. FDA noted that a complete EA that addresses ESA concerns adequately is also key to its review.

Post-meeting Notes: Next Steps per Oxitec/Intrexon from the company's feedback on Mon May 22:
1) Oxitec agreed to provide a list of data it intends to submit to support an EUP and timeframes for submission
2) EPA committed to reviewing the list of data and timeframes presented by Oxitec with a view to determining which data were critical at the time of EUP application submission